Inf rmation Discl sur

Statement By Applicant

(Use Several Sheets if Necessary)

Docket: 093/005

U.S.S.N. To be assigned

Title: Hepatocytes for Therapy and Drug Screening

made from Embryonic Stem Cells Inventors: Rambhatla, L., et al.

Filing Date: March 1, 2002

Group: 1632

6U.S. Pat nt D cum nts

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Examiner Initial	Ref.	Patent No.	Filing Date	Issue Date	Class/ Subclass	Inventors:	Title:
TMT	A	5,030,105	11/15/89	7/9/91	435/29	Kurl-Harcuch, W., et al.	Process For The Long-Term Surviving Culture Of Hepatocytes
7	В	5,532,156	10/8/93	7/2/96	435/240.2	Talbot, N., et al.	Hepatocyte Cell Line Derived From The Epiblast Of Pig Blastocysts
	С	5,559,022	1/26/95	9/24/96	435/240.2	Naughton, B.A., et al.	Liver Reserve Cells
	D	5,576,207	6/24/94	11/19/96	435/240.2	Reid, L.M., et al.	Method O Expanding Hepatic Precursor Cells
	E	5,763,255	1/25/95	6/9/98	435/240.23	Swiderek, M.S., et al.	Inducing Epithelial Cell Differentiation With Dried Native Fibrillar Collagen
	F	5,869,243	3/5/96	2/9/99	435/6	Jauregui, H.O., et al.	Immortalized Hepatocytes
 	G	6,017,760	10/10/95	1/25/00	435/378	Jauregui, H.O., et al.	Isolation and Culture Of Porcine Hepatocytes

Foreign Patent or Published Foreign Patent Application Translation Document Publ. Juris-Examiner Ref. No diction Date Initial No. Embryonic Stem Cells Capable Of Differentiating Into PCT 5/11/95 WO 95/12665 Н TNT Desired Cell Lines Use Of Histone Deacetylase Inhibitors To Activate 12/18/97 **PCT** WO 97/47307 Transgene Expression Use Of Histone Deacetylase Inhibitors For Treating EP 0 827 742 3/11/98 ΕP Fribosis Or Cirrhosis A1 Use Of Histone Decarboxylase Inhibitors For Treating EP 0 827 743 3/11/98 ΕP K **Fibrosis** Methods For The Use Of Inhibitors Of Co-Repressors PCT WO 99/23885 5/20/99 L For The Treatment Of Neoplastic Diseases PCT Transcription Therapy For Cancers WO 99/37150 7/29/99 М Cell Culturing Method And Medium For Producing EP 0 953 633 11/3/99 EP Ν Proliferated, Normal, Differentiated Human Liver Cells A1 1/20/00 **PCT** Liver Stem Cell 0 WO 00/03001 Reversibly Immortalized Hepatocytes And Methods Of 4/6/00 **PCT** Ρ WO 00/18239 Porcine Oocytes with Improved Developmental **PCT** WO 00/22098 4/20/00 Q Competence PCT **Human Liver Progenitors** WO 00/43498 7/27/00 TNT R

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Examiner: Initial if citation considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. **Includ c py f this f rm with next communicati n t applicant.**PTO-1449 — Page 1

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Oth r D cuments

Examiner Initial	Ref.	Author, Title, Source, Date
TNT	S	Adams, R.M., et al., "Effective cryopreservation and long-term storage of primary human hepatocytes with recovery of viability, differentiation, and replicative potential", Cell Transplantation, 4(6):579-586 (1995)
	Т	Agelli, M., et al., "Putative liver progenitor cells: conditions for long-term survival in culture", <i>Histochemical Journal</i> , 29:205-217 (1997)
	U	Alison, M., "Liver stem cells: a two compartment system", Cell Biology, 10:710-715 (1998)
	٧	Baribault, H., et al., "Dexamethasone and dimethylsulfoxide as distinct regulators of growth and differentiation of cultured suckling rat hepatocytes", <i>J Cell Physiol</i> , 129 (1):77-84 (1986)
	w	Block, G.D., et al., "Population expansion, clonal growth, and specific differentiation patterns in primary cultures of hepatocytes induced by HGF/SF, EGF and TGF∝ in a chemically defined (HGM) medium", <i>J Cell Bio.</i> , 132(6)11331149 (1996)
	х	Blouin, MJ., et al., "Specialization switch in differentiating embryonic rat liver progenitor cells in response to sodiur butyrate", Exp Cell Res, 217(1):22-30 (1995)
·	Υ	Brill, S., et al., "Expansion conditions for early hepatic progenitor cells from embryonal and neonatal rat livers", Dig Diseases & Sci, 44(2):364-371 (2/99)
	Z	Buommino, E., et al., "Sodium butyrate/retinoic acid costimulation induces apoptosis-independent growth arrest and cell differentiation in normal and ras-transformed seminal vesicle epithelial cells unresponsive to retinoic acid" <i>J Mol Endocrinol</i> 24(1):83-94 (2/00)
	AA	Chen, WY., et al., "Reactivation of silenced, virally transduced genes by inhibitors of histone deacetylase", <i>Proc. Natl. Acad. Sci. USA</i> , 94 :5798-5803 (5/97)
	AB	Coghlan, A., "Highly Cultured", New Scientist, Aug. 19, 2000
	AC	Coleman W.B., et al., "Development of dexamethasone-inducible tyrosine aminotransferase activity in WB-F344 reliver epithelial stemlike cells cultured in the presence of sodium butyrate", J Cell Physiol, 161(3):463-469 (12/94)
	AD	Davis, MG., et al., "Involvement of gialpha2 in sodium butyrate-induced erythroblastic differentiation of K562 cells" Biochem J, 1(346)Pt2:455-461 (3/00)
	AE	Devereux, T.R., et al., "DNA methylation analysis of the promoter region of the human telomerase reverse transcriptase (hTERT) gene", Cancer Research, 59:6087-6090,(12/99)
	AF	Enat, R., et al., "Hepatocyte proliferation in vitro: Its dependence on the use of serum-free hormonally defined medium and substrata of extracellular matrix", <i>Proc. Natl. Acad. Sci. USA</i> , 81 :1411-1415 (3/84)
	AG	Engelmann, G.L., et al., "Effect of sodium butyrate on primary cultures of adult rat hepatocytes", In Vitro Cell Dev Biol., 23(2):86-92 (2/87)
	АН	Falasca, L., et al., "The effect of retinoic acid on the re-establishment of differentiated hepatocyte phenotype in primary culture", Cell Tissue Res., 293:337-347 (1998)
	Al	Germain, L., et al., "Biliary epithelial and hepatocytic cell lineage relationships in embryonic rat liver as determined by the differential expression of cytokeratins, ∝-fetoprotein, albumin, and cell surface-exposed components" Cancer Res, 48:4909-4918 (9/88)
	AJ	Germain, L., et al., "Promotion of growth and differentiation of rat ductular oval cells in primary culture", Cancer Res, 48(2):368-378 (1988)
	AK	Gillenwater, A., et al., "Effects of sodium butyrate on growth, differentiation, and apoptosis in head and neck squarnous carcinoma cell lines", Head Neck, 22(3):247-256 (5/00)
	AL	Gladhaug, I.P., et al., "Effects of butyrate on epidermal growth factor receptor binding, morphology, and DNA synthesis in cultured rate hepatocytes", Cancer Res, 48(22):6560-6564 (11/15/88)
TNT	AM	Graham, K.A., et al., "Sodium butyrate induces differentiation in breast cancer cell lines expressing the estrogen receptor", <i>J Cell Physiol</i> , 136 (1):63-71 (7/88)

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TNT	AN	Grisham, J.W., et al., "Liver stem cells", Stem Cells, 233-282 (1997)
	AO	Guixiang, T., et al., "Different effects of cyclic AMP and butyrate on eosinophilic differentiation, apoptosis and bcl-2 expression of a human eosinophilic leukemia cell line, EoL-1", Hematol Oncol, 14(4):181-92 (12/96)
	AP	Jeng, J.H., et al., "Effects of butyrate and propionate on the adhesion, growth, cell cycle kinetics, and protein synthesis of cultured human gingival fibroblasts", <i>J Periodontol</i> , 70 (12):1435-1442 (12/99)
	AQ	Kamitani, H., et al., "Regulation of 12-lipoxygenase in rat intestinal epithelial cells during differentiation and apoptosis induced by sodium butyrate", Arch Biochem Biophys, 368(1):45-55 (8/1/99)
	AR	Kosugi, H., et al., "Histone deacetylase inhibitors are the potent inducer/enhancer of differentiation in acute myeloic leukemia: a new approach to anti-leukemia therapy", <i>Leukemia</i> , 13:1316-1324 (1999)
	AS	Lazaro, C.A., et al., "Generation of hepatocytes from oval cell precursors in culture", Cancer Res, 58:5514-5522 (12/1/98)
	AT	Li, J., et al., "Mammalian hepatocyte differentiation requires the transcription factor HNF-4x", Genes & Dev, 14:464-474 (2000)
	AU	Matsui, T., et al., "Induction of catecholamine synthesis in human neuroblastoma cells by replication inhibitors and sodium butyrate", <i>Brain Res</i> , 843 (1-2):112-117 (10/2/99)
	AV	McBain, J., et al., "Apoptotic death in adenocarcinoma cell lines induced by butyrate and other histone deacetylase inhibitors", <i>Biochem Pharm</i> , 53:1357-1368 (1997)
	AW	Michalopoulos, G.K., et al., "Morphogenetic events in mixed cultures of rat hepatocytes and nonparenchymal cells maintained in biological matrices in the presence of hepatocyte growth factor and epidermal growth factor", Hepatology, 29(1):90-100 (1999)
	AX	Mitaka, T., et al., "Redifferentiation of proliferated rat hepatocytes cultured in L15 medium supplemented with EGF and DMSO", In Vitro Cell Dev. Biol., 29A:714-722 (9/93)
	AY	Mitaka, T., "The current status of primary hepatocyte culture", Int. J. Exp. Path, 79:393-409 (1998)
	AZ	Niki, T., et al., "A histone deacetylase Inhibitor, trichostatin A, suppresses myofibroblastic differentiation of rat hepatic stellate cells in pirnary culture", <i>Hepatology</i> , 29 (3):858-867 (1999)
	BA	Pack, R., et al., "Isolation, biochemical characterization, long-term culture, and pheotype modulation of oval cells from carcinogen-fed rats", Exp Cell Res, 204(2):198-209 (1993)
	ВВ	Pagan, R., et al., "Effects of growth and differentiation factors on the epithelial-mesenchymal transition in cultured neonatal rat hepatocytes", <i>J of Hepatology</i> , 31:859-904 (1999)
	ВС	Perez, R., et al., "Sodium butyrate upregulates Kupffer cell PGE2 production and modulates immune function", J Surg Res, 78(1):1-6 (7/15/98)
	BD	Perrine, SP., et al., "A short-term trial of butyrate to stimulate fetal-globin-gene expression in the beta-globin disorders", N Engl J Med, 328(2):81-86, (1/14/93)
	BE	Perrine, SP., et al., "Butyrate derivatives. New agents for stimulating fetal globin production in the beta-globin disorders", Am J Pediatr Hemotol Oncol, 16(1):67-71 (2/94)
	BF	Reynolds, S., et al., "Differentiation-inducing effect of retinoic acid, difluoromethylomithine, sodium butyrate and sodium suramin in human colon cancer cells", Cancer Lett, 134(1):53-60 (12/11/98)
	BG	Rivero JA., et al., "Sodium butyrate stimulates PKC activation and induces differential expression of certain PKC isoforms during erythroid differentiation", <i>Biochem Biophys Res Commun</i> , 248 (3):664-668 (7/30/98)
	ВН	Rocchi, P., et al., "Effect of butyrate analogues on proliferation and differentiation in human neuroblastoma cell lines", Anticancer Res, 18(2A):1099-103 (3/98)
TNT	ВІ	Rogler, LE., "Selective bipotential differentiation of mouse embryonic hepatoblasts in vitro", Am J Pathol, 150(2):591-602 (1997)

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TIT	BJ	Runge, D., et al., "STAT 1 alpha/1 beta, STAT 3 and STAT 5: Expression and Association with c-MET and EGF-Receptor in Long-Term Cultures of Human Hepatocytes", <i>Biochemical and Biophysical Research Communications</i> , 265:376-381 (1999)
	ВК	Saito, H., et al., "Differentiating effect of sodium butyrate on human hepatoma cell lines PLC/PRF/5, HCC-M and HCC-T", Int J Cancer, 48(2):291-296 (5/10/91)
	BL	Sanchez, A., et al., "Transforming growth factor-B (TGF-B) and EGF promote cord-like structures that indicate terminal differentiation of fetal hepatocytes in primary culture", Exp Cell Res, 242:27-37 (1998)
i	ВМ	Schultz, RM., et al., "Reprogramming of gene expression during preimplantation development", <i>J of Exp Zoology</i> (Mol Dev Evol), 285 :276-282 (1999)
	BN	Siavoshian, S., et al., "Butyrate and trichostatin A effects on the proliferation/differentiation of human intestinal epithelial cells: induction of cyclin D3 and p21 expression", Gut, 46(4):507-14 (4/2000)
	во	Sirnon, B., et al., "Transient transcriptional activation of gastrin during sodium butyrate-induced differentiation of islet cells", Regul Pept, 70(2-3):143-8 (6/18/97)
	ВР	Staecker, JL., et al., "Stimulation of DNA synthesis in primary cultures of adult rat hepatocytes by sodium butyrate", Biochem Biophys Res Commun, 147(1):78-85 (8/87)
	BQ	Staecker, JL., et al., "The effect of sodium butyrate on tyrosine aminotransferase induction in primary cultures of normal adult rat hepatocytes", <i>Arch Biochem Biophys</i> , 261 (2):291-8 (3/88)
	BR	Staecker, JL., et al., "Sodium butyrate preserves aspects of the differentiated phenotype of normal adult rat hepatocytes in culture", <i>J Cell Physiol</i> , 135(3):367-76 (1988)
	BS	Strain, A., "Ex vivo liver cell morphogenesis: one step nearer to the bioartificial liver", Hepatology, 29(1):288-290 (1/99)
	вт	Sun, SH., et al., "Altered phospholipid metabolism in sodium butyrate-induced differentiation of C6 glioma cells", Lipids, 32(3):273-82 (3/97)
	BU	Tamagawa, K., et al., "Proanthocyanidins from barley bran potentiate retinoic acid-induced granulocytic and sodium butyrate-induced monocytic differentiation of HL60 cells", <i>Biosci Biotechnol Biochem</i> , 62 (8):1483-7 (8/98)
	в٧	Tanaka, T., et al., "Adenovirus-mediated prodrug gene therapy for carcinoembryonic antigen-producing human gastric carcinoma cells in vitro", Cancer Res, 56(6):1341-5 (3/96)
	BW	Tateno, C., et al., "Growth and differentiation of adult rat hepatocytes regulated by the interaction between parenchymal and non-parenchymal liver cells", <i>J of Gasto and Hepatology</i> , 13:S83-92 (1998)
	вх	Tateno, C., et al., "Growth potential and differentiation capacity of adult rat hepatocytes in vitro", Wound Repair and Regeneration, 7(1):36-44 (1999)
	BY	Wang, G., et al., "Transforming growth factor-beta 1 acts cooperatively with sodium n-butyrate to induce differentiation of normal human keratinocytes", Exp Cell Res, 198(1):27-30 (1/92)
TNT	BZ	Watkins, SM., et al., "Butyric acid and tributyrin induce apoptosis in human hepatic tumour cells", <i>J Dairy Res</i> , 66(4):559-67 (11/99)

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THT	CA	Yabushita, H., et al., "Effects of sodium butyrate, dimethylsulfoxide and dibutyryl cAMP on the poorly differentiated ovarian adenocarcinoma cell line AMOC-2", Oncol Res, 5(4-5):173-82 (1993)		
	СВ	Yamada, K., et al., "Effects of butyrate on cell cycle progression and polyploidization of various types of mammalian cells", Biosci Biotechnol Biochem, 56(8):1261-5 (8/92)		
	СС	Yoon, J-H., et al., "Augmentation of Urea-synthetic Capacity by Inhibition of Nitric Oxide Synthesis in Butyrate- Induced Differentiated Human Hepatocytes", FEBS Letters, 474:175-178 (2000)		
	CD	Yoon, J-H., et al., "Development of a non-transformed human liver cell line with differentiated-hepatocyte a synthetic functions: applicable for bioartificial liver", Int. J. of Artifical Organs, 22:769-777(1999)		
	CE	Yoshizawa, T., et al., "Dimethylsulfoxide maintains intercellular communication by preserving the gap junctional protein connexin32 in primary cultured hepatocyte doublets from rats", J of Gastro and Hepat, 12:325-330 (1997)		
TNT	CF	Zvibel, I., et al., "Phenotypic characterization of rat hepatoma cell lines and lineage-specific regulation of gene expression by differentiation agents", Differentiation, 63:215-223 (1998)		

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